

Amendments to the Claims

Claims 1-85 (Canceled).

Claim 86 (New). A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity, comprising:

- (a) providing a host cell that expresses a recombinant antibody comprising an Fc region containing N-linked oligosaccharides;
- (b) glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltransferase;
- (c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and
- (d) isolating said recombinant antibody;

wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered.

Claim 87 (New). A method for producing a recombinant antibody having increased Fc receptor binding affinity, comprising:

- (a) providing a host cell that expresses a recombinant antibody comprising an Fc region containing N-linked oligosaccharides;
- (b) glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltransferase;
- (c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and
- (d) isolating said recombinant antibody;

wherein said recombinant antibody has increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered.

Claim 88 (New). A method according to claim 86 or claim 87, wherein said activity is increased.

Claim 89 (New). A method according to claim 86 or claim 87, wherein said activity is decreased.

Claim 90 (New). A method according to claim 86 or claim 87, wherein said at least one glycoprotein-modifying glycosyl transferase is selected from the group consisting of: $\beta(1,4)$ -N-acetylglucosaminyltransferase III, $\beta(1,4)$ -N-acetylglucosaminyltransferase V, $\beta(1,4)$ - galactosyltransferase, α -mannosidase II, and core α -1,6-fucosyltransferase.

Claim 91 (New). A method according to claim 90, wherein said at least one glycoprotein-modifying glycosyl transferase is $\beta(1,4)$ -N-acetylglucosaminyltransferase III.

Claim 92 (New). A method according to claim 90, wherein said at least one glycoprotein-modifying glycosyl transferase is $\beta(1,4)$ - galactosyltransferase.

Claim 93 (New). A method according to claim 90, wherein said at least one glycoprotein-modifying glycosyl transferase is α -mannosidase II.

Claim 94 (New). A method according to claim 90, wherein said at least one glycoprotein-modifying glycosyl transferase is core α -1,6-fucosyltransferase.

Claim 95 (New). A method according to claim 90, wherein said at least one glycoprotein-modifying glycosyl transferase is $\beta(1,4)$ -N-acetylglucosaminyltransferase III and α -mannosidase II.

Claim 96 (New). A method according to claim 90, wherein said at least one glycoprotein-modifying glycosyl transferase is $\beta(1,4)$ -N-acetylglucosaminyltransferase III and α -mannosidase II and $\beta(1,4)$ -galactosyltransferase.

Claim 97 (New). A method according to claim 90, wherein said activity is expression of said at least one glycoprotein-modifying glycosyl transferase.

Claim 98 (New). A method according to claim 91, wherein expression of said $\beta(1,4)$ -N-acetylglucosaminyltransferase III is increased.

Claim 99 (New). A method according to claim 93, wherein expression of said α -mannosidase II is increased.

Claim 100 (New). A method according to claim 95, wherein expression of both said $\beta(1,4)$ -N-acetylglucosaminyltransferase III and said α -mannosidase II is increased.

Claim 101 (New). A method according to claim 94, wherein the activity of said core α -1,6-fucosyltransferase is decreased.

Claim 102 (New). A method according to claim 86 or claim 87, wherein said glycoengineering comprises introducing into said host cell at least one polynucleotide encoding an exogenous glycoprotein-modifying glycosyl transferase.

Claim 103 (New). A method according to claim 102, wherein said exogenous glycoprotein-modifying glycosyl transferase is $\beta(1,4)$ -N-acetylglucosaminyltransferase III.

Claim 104 (New). A method according to claim 102, wherein said exogenous glycoprotein-modifying glycosyl transferase is α -mannosidase II.

Claim 105 (New). A method according to claim 102, wherein said exogenous glycoprotein-modifying glycosyl transferase is $\beta(1,4)$ -N-acetylglucosaminyltransferase III and α -mannosidase II.

Claim 106 (New). A method according to claim 86 or claim 87, wherein said host cell is selected from the group consisting of an engineered CHO cell, an engineered BHK cell, an engineered NS0 cell, an engineered SP2/0 cell, an engineered yeast cell, and an engineered plant cell.

Claim 107 (New). A method according to claim 106, wherein said host cell is an engineered CHO cell.

Claim 108 (New). A method according to claim 86 or claim 87, wherein said recombinant antibody has an increased proportion of nonfucosylated oligosaccharides in the Fc region as a result of said glycoengineering compared to the corresponding antibody produced by the same host cell that has not been glycoengineered.

Claim 109 (New). A method according to claim 86 or claim 87, wherein the predominant N-linked oligosaccharide in the Fc region of the antibody produced by said glycoengineered host cell is nonfucosylated.

Claim 110 (New). A method according to claim 86 or claim 87, wherein said recombinant antibody is a chimeric antibody.

Claim 111 (New). A method according to claim 86 or claim 87, wherein said recombinant antibody is a humanized antibody.

Claim 112 (New). A method according to claim 86 or claim 87, wherein said recombinant antibody is an antibody fragment that contains a Fc region.

Claim 113 (New). A method according to claim 86 or claim 87, wherein said recombinant antibody is a fusion protein that includes a Fc region of an immunoglobulin.

Claim 114 (New). A method according to claim 86 or claim 87, wherein the predominant N-linked oligosaccharide in the Fc region of said antibody produced by said glycoengineered host cell is not a high-mannose structure.

Claim 115 (New). A method according to claim 86 or claim 87, wherein the Fc region containing N-linked oligosaccharides in said antibody further comprises an increased proportion of GlcNAc residues compared to the corresponding antibody produced by the same host cell that has not been glycoengineered.

Claim 116 (New). A method according to claim 86 or claim 87, wherein said antibody produced by said glycoengineered host cell has an increased proportion of GlcNAc residues in the Fc region relative to the proportion of fucose residues compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein said antibody has increased Fc-mediated cellular cytotoxicity as a result of said glycoengineering.

Claim 117 (New). A method according to claim 116, wherein said GlcNAc residues are bisecting.

Claim 118 (New). A method according to claim 116, wherein said GlcNAc residues are bisecting and wherein said bisected oligosaccharides are of complex type.

Claim 119 (New). A method according to claim 116, wherein said GlcNAc residues are bisecting and wherein said bisected oligosaccharides are of hybrid type.

Claim 120 (New). A method according to claim 86 or claim 87, wherein said antibody is a therapeutic antibody.

Claim 121 (New). A method according to claim 86 or claim 87, wherein said antibody selectively binds to an antigen expressed by a cancer cell.

Claim 122 (New). A method according to claim 114, wherein said antibody is a monoclonal antibody.

Claim 123 (New). A method according to claim 120, wherein said antibody is selected from the group consisting of: an anti-CD20 antibody, an anti-human neuroblastoma antibody, an anti-human renal cell carcinoma antibody, an anti-HER2 antibody, an anti-human colon, lung, and breast carcinoma antibody, an anti-human 17-1A antigen antibody, a humanized anti-human colorectal tumor antibody, an anti-human melanoma antibody, and an anti-human squamous-cell carcinoma antibody.

Claim 124 (New). A method according to claim 120, wherein said antibody is an IgG.

Claim 125 (New). A method according to claim 86 or claim 87, wherein the majority of the N-linked oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are bisected.

Claim 126 (New). A method according to claim 86 or claim 87, wherein the majority of the N-linked oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are nonfucosylated.

Claim 127 (New). A method according to claim 86 or claim 87, wherein the majority of the N-linked oligosaccharides in said Fc region of said antibody produced by said glycoengineered host cell are bisected, nonfucosylated.

Claim 128 (New). A method according to claim 114, wherein said antibody is a therapeutic monoclonal antibody having a human Fc region and that selectively binds an antigen expressed by cancer cells, and wherein the majority of oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are nonfucosylated.

Claim 129 (New). A method according to claim 86 or claim 87, wherein at least 45% of the oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are complex structures.

Claim 130 (New). A method according to claim 86 or claim 87, wherein said recombinant antibody produced by said glycoengineered host cell exhibits at least an 80% increase in maximal ADCC activity compared to the same antibody produced by the same host cell under identical culture and purification conditions, but which has not been glycoengineered.

Claim 131 (New). A method according to claim 86 or 87, wherein said at least one glycoprotein-modifying glycosyl transferase is mammalian.

Claim 132 (New). A method according to claim 131, wherein said at least one glycoprotein-modifying glycosyl transferase is human.

Claim 133 (New). A method for lysing a target cell, said method comprising contacting said target cell with an antibody prepared by the method of claim 86 or claim 87.

Claim 134 (New). A method according to claim 133, wherein said recombinant antibody produced by said glycoengineered host cell has an increased proportion of nonfucosylated oligosaccharides in the Fc region compared to the corresponding antibody produced by the same host cell that has not been glycoengineered.

Claim 135 (New). A method according to claim 133, wherein the predominant N-linked oligosaccharide in the Fc region of said antibody produced by said glycoengineered host cell is nonfucosylated.

Claim 136 (New). A method according to claim 133, wherein said antibody is a chimeric antibody.

Claim 137 (New). A method according to claim 133, wherein said antibody is a humanized antibody.

Claim 138 (New). A method according to claim 133, wherein said antibody is an antibody fragment that contains a Fc region.

Claim 139 (New). A method according to claim 133, wherein said antibody is a fusion protein that includes a Fc region of an immunoglobulin.

Claim 140 (New). A method according to claim 133, wherein the predominant N-linked oligosaccharide in the Fc region of said antibody produced by said glycoengineered host cell is not a high-mannose structure.

Claim 141 (New). A method according to claim 133, wherein the Fc region containing N-linked oligosaccharides of the antibody produced by said glycoengineered host cell further comprises an increased proportion of GlcNAc residues compared to the corresponding antibody produced by the same host cell that has not been glycoengineered.

Claim 142 (New). A method according to claim 133, wherein said antibody produced by said glycoengineered host cell has an increased proportion of GlcNAc residues in the Fc region relative to the proportion of fucose residues compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein said antibody has increased Fc-mediated cellular cytotoxicity as a result of said glycoengineering.

Claim 143 (New). A method according to claim 142, wherein said GlcNAc residues are bisecting.

Claim 144 (New). A method according to claim 142, wherein said GlcNAc residues are bisecting and wherein said bisected oligosaccharides are of complex type.

Claim 145 (New). A method according to claim 142, wherein said GlcNAc residues are bisecting and wherein said bisected oligosaccharides are of hybrid type.

Claim 146 (New). A method according to claim 133, wherein said antibody is a therapeutic antibody.

Claim 147 (New). A method according to claim 133, wherein said antibody selectively binds to an antigen expressed by cancer cells.

Claim 148 (New). A method according to claim 133, wherein said antibody is a monoclonal antibody.

Claim 149 (New). A method according to claim 133, wherein said antibody is selected from the group consisting of: an anti-CD20 antibody, an anti-human neuroblastoma antibody, an anti-human renal cell carcinoma antibody, an anti-HER2 antibody, an anti-human colon, lung, and breast carcinoma antibody, an anti-human 17-1A antigen antibody, a humanized anti-human colorectal tumor antibody, an anti-human melanoma antibody, and an anti-human squamous-cell carcinoma antibody.

Claim 150 (New). A method according to claim 133, wherein said antibody is an IgG.

Claim 151 (New). A method according to claim 133, wherein the majority of the N-linked oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are bisected.

Claim 152 (New). A method according to claim 133, wherein the majority of the N-linked oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are nonfucosylated.

Claim 153 (New). A method according to claim 133, wherein the majority of the N-linked oligosaccharides in said Fc region of said antibody produced by said glycoengineered host cell are bisected, nonfucosylated.

Claim 154 (New). A method according to claim 133, wherein said antibody produced by said glycoengineered host cell is a therapeutic monoclonal antibody having a human Fc region and that selectively binds an antigen expressed by cancer cells, and wherein the majority of oligosaccharides in the Fc region of said antibody are nonfucosylated.

Claim 155 (New). A method according to claim 133, wherein at least 45% of the oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are complex structures.

Claim 156 (New). A method according to claim 133, wherein said recombinant antibody produced by said glycoengineered host cell exhibits at least an 80% increase in maximal ADCC activity compared to the same antibody produced by the same host cell under identical culture and purification conditions, but which has not been glycoengineered.

Claim 157 (New). A method according to claim 157, wherein said at least one glycoprotein-modifying glycosyl transferase is mammalian.

Claim 158 (New). A method according to claim 127, wherein said at least one glycoprotein-modifying glycosyl transferase is human.

Claim 159 (New). A method according to claim 86 or claim 87, wherein said glycoengineering comprises genetically manipulating said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltransferase.

Claim 160 (New). A method according to claim 121, wherein said antigen is differentially expressed by said cancer cell.

Claim 161 (New). A method according to claim 133, wherein said target cell is a tumor cell.

Claim 162 (New). A method according to claim 161, wherein said antibody specifically binds an antigen differentially expressed on said target cell.